UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

REGION VII
901 NORTH 5TH STREET
KANSAS CITY, KANSAS 66101

APR 24 2006

MEMORANDUM

SUBJECT: Review of Bioavailability Memorandum
Herculaneum Lead Smelter Site
Herculaneum, Missouri

FROM: Mike Beringer
Toxicologist
ENSV/DISO

TO: Bruce Morrison
Remedial Project Manager
SUPR/FFSE

As requested, we have reviewed the memorandum from the Doe Run Company (Doe Run), dated March 21, 2006, regarding soil and dust lead bioavailability at the Herculaneum Lead Smelter Site. Our comments are limited to evaluating whether Doe Run's proposed approach is consistent with U.S. Environmental Protection Agency (EPA) lead risk assessment guidance, as we did not review the underlying studies referenced in this memorandum. If you have any questions concerning the attached comments, please let me know.

Comments

1. **Page 1, par. 1** It is technically inaccurate to state that *in vitro* models measure bioavailability. Rather, *in vitro* tests measure the rate or extent of solubilized lead in an extraction solvent that resembles gastric fluid This solubilized fraction should be referred to as *in vitro* bioaccessibility (IVBA), which may be an indicator of *in vivo* relative bioavailability (RBA). Doe Run should use the term "*in vitro* bioaccessibility" in the risk assessment text and figures to ensure this concept is accurately characterized.

2. ***In Vitro* Study Results (p. 2)** This section examines various relationships between IVBA and other parameters such as lead concentration and distance from the smelter. While these evaluations have merit, the conclusions are qualitative in nature (e.g., "strong relationship") and are not supported by any statistical tests. Doe Run should provide documentation of the statistical analyses of these relationships in an Appendix to the risk assessment, unless these relationships will not be discussed in the document.

A717 2.0

ALCO

3. **Slag storage pile (p. 5)** EPA's current policy is that *in vivo* bioassays (e.g., juvenile swine) are the only approach for quantitatively measuring and adjusting default bioavailability in site-specific lead risk assessments (EPA, 1999). Because an *in vitro* bioaccessibility test has not yet been validated with *in vivo* data for lead, the risk assessment must use the default absolute bioavailability of 12% when evaluating an adolescent trespasser on the slag pile. The IVBA results can be used to characterize the uncertainty with using the default value.

4. **Slag storage pile (p. 5)** Region 7 also notes that the juvenile swine model was developed for predicting RBA in human children. As a result, the risk assessment should acknowledge there is additional uncertainty when using *in vivo* bioavailability estimates for adolescents and adults because evidence exists to indicate that absolute bioavailability of soluble lead (e.g., in food or water) varies with age.

5. **Additional *in vitro* results (p. 5)** Region 7 agrees that the 77% bioaccessibility estimate is significantly higher than the other three reported values. However, the risk assessment should also acknowledge that this result may not be an "outlier," but represents the full range of roadway dust bioavailability in Herculaneum.

6. ***In Vivo* Study Results (p. 6)** Region 7 does not agree entirely with the statement that it is "unlikely if not impossible" for lead in Herculaneum soils to be more bioavailable than soluble lead. While it is unlikely, it is not impossible for lead in soil to be more bioavailable than lead acetate. Also, Region 7 points out that the occurrence of a measured RBA value above 1.0 cannot be attributed solely to animal variability, but would likely be a result of several sources of measurement error such as analytical and statistical uncertainty. It is also possible that measured RBA values may be too low (e.g., liver) as a result of measurement error. The overall impact is reduced by using the mean of four endpoint-specific RBA values. Any discussion of this issue in the risk assessment should be presented in a balanced fashion.

7. **Comparison of *In Vitro* and *In Vivo* Estimates (p. 6)** In comparing the IVBA and *in vivo* RBA estimates for soil and dust, Doe Run is making an assumption that the *in vitro* method yields results identical to *in vivo* values (i.e., one-to-one relationship). However, EPA's analysis of 19 test materials shows the best fit linear correlation between *in vivo* RBA and IVBA values yields the following equation:

$$RBA = 1.03(IVBA) - 0.06$$

This analysis is part of EPA's efforts to validate a specific *in vitro* test method for lead which is currently undergoing external peer review. Because the equation is based on samples collected primarily from mining and milling sites, it is plausible that some forms of lead might not follow the observed correlation. Our initial evaluation indicates the samples evaluated for IVBA at the Herculaneum Lead Smelter Site would fall within the range of soil types and lead phases evaluated as part of the correlation analysis. Thus, Region 7

recommends using this mathematical equation to estimate *in vivo* RBA. The resulting values should be used when comparing results from the two test methods and also when characterizing the potential variability in bioavailability across the site.

8. **Comparison of *In Vitro* and *In Vivo* Estimates (p. 6)** This section identifies three possible options for selecting an RBA estimate based on *in vivo* and *in vitro* results. But as discussed in Comment #3, only site-specific *in vivo* studies can be used to replace the default bioavailability values in lead risk assessments. The *in vivo* RBA estimates for soil (97%) and dust (52%) must be used in the risk assessment because they currently represent the best measure of oral uptake in young children at the Herculaneum Lead Smelter Site. The IVBA results should be addressed when discussing the uncertainties of the risk assessment, particularly in the case of dust where the results bracket the *in vivo* result of 52%.

9. **Comparison of *In Vitro* and *In Vivo* Estimates (p. 7)** Region 7 does not agree that it is appropriate to round all RBA estimates to one significant figure because of uncertainty. While we agree there is uncertainty as well as variability in the actual RBA values, EPA does not address this inherent uncertainty and variability by rounding all values to one significant figure. Rather, the range of bioavailability estimates should be fully characterized in the risk assessment and the uncertainties associated with each step of the risk assessment process discussed.

References

U.S. EPA. 1999. Short Sheet: IEUBK Model Bioavailability Variable. Office of Solid Waste and Emergency Response, Washington, D.C. EPA/540-F-00-006.